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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/662,783	09/12/2000	Richard A. Shimkets	15966-577 (CURA-77)	3145

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/662,783	SHIMKETS ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 66-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 66-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 09 March 2005 is acknowledged and entered. Following the amendment, claims 1, 2 and 66-71 are amended, and the new claims 72 and 73 are added.

Currently, claims 1, 2, and 66-73 are pending and under consideration.

Withdrawal of Objections and Rejections:

The new matter rejection of claims 2, 66 and 71 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's amendment.

The scope of enablement rejection of claims 1, 2, and 66-69 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's argument.

The prior art rejection of claim 71 under 35 U.S.C. 102(e) as being anticipated by Gilbert et al., US 6,495,668 B1, is withdrawn in view of applicant's amendment.

Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, and 66-71 remain rejected, and the new claims 72 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 remains indefinite for the recitation of "polypeptide dimer consisting of peptides consisting of:" ... (fragment I), ... (fragment II), *and* ... (fragment III). It is unclear how a polypeptide dimer can have all three peptides, or if the complex has all three peptides, it would not be a *dimer*. Claim 69 is similarly indefinite.

Claim 72 is indefinite because it is unclear what "the peptide residues 247-370 of SEQ ID NO:2 are in the form of a bonded polypeptide of ... *and* ..." is meant, and whether they are one or two polypeptides. Claim 73 is similarly indefinite.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 70 and 71 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a polypeptide dimer of SEQ ID NO:2, wherein one polypeptide chain of the dimer comprises peptide fragments of 16 kDa and 5-6 kDa, which are amino acids 247-338 and 339-370 of SEQ ID NO:2, respectively, does not reasonably provide enablement for claims to a polypeptide dimmer, wherein one polypeptide chain comprising any or all peptide fragments of 16 kDa and 5-6 kDa of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the last Office Action mailed on 09 September 2004.

Applicants argument filed on 09 March 2005 has been fully considered, but is not deemed persuasive for reasons below.

At page 5 of the response, the applicant argues that there are a total of only 2 possible combinations of dimers that can be encompassed by these claims, namely 16 kDa portion with a 22-25 kDa portion, and a 5-6 kDa portion with a 22-25 kDa portion, and that it would not take an undue amount of experimentation to determine whether each combination retains functional activity. This argument is not persuasive for the following reasons. First, contrary to applicants interpretation, claim 70, as written, reads on that the first peptide consists of both 16 kDa and 5-6 kDa, i.e., both are coupled with the second peptide of 22-25 kDa. Further, as the peptide fragments are defined by their molecular weight rather than their sequence structure, there would be hundreds of possibilities as to the sequence structure of 16 kDa and 5-6 kDa fragments. The specification merely discloses one of such possibilities, i.e., fragments of amino acids 247-338 and 339-370 of SEQ ID NO:2, corresponding to 16 kDa and 5-6 kDa, respectively, and provides no guidance or other working examples as to how to make all polypeptide dimers encompassed by the claims, and to predict the desired functional activity. As such, undue experimentation would be required to make and/or use the claimed invention in its full scope.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, and 66-70 remain rejected, and the new claims 72 and 73 are rejected under 35 U.S.C. 102(e) as being anticipated by Gilbert et al., US 6,495,668 B1, for the reasons of record set forth in the previous Office Actions mailed on 6/24/03, 1/24/04, and 9/9/04.

Applicants argument filed on 09 March 2005 has been fully considered, but is not deemed persuasive for reasons below.

At pages 6-7 of the response, the applicant argues that applicants show in Example 12 that under reducing conditions SDS-PAGE clearly indicates three bands having molecular weight of 22-25, 16, and 5-6 kDa, respectively, that bands I and II begin at residue 247 and band III begins at residue 339, and that nowhere does Gilbert disclose such peptide fragments, nor the dimer thereof. This argument is not persuasive because, as addressed in the last Office Action, Gilbert clearly teaches peptide dimers comprising, among others, the polypeptide chains identical to that of the present invention, i.e., the peptide dimer comprising polypeptide fragments of 247-370 of the present SEQ ID NO:2 (claim 1, and column 7, lines 23-25). Gilbert teaches that each of said first and second polypeptides is from 113-118 amino acid residues in length (claim 6), that is the polypeptide fragment may start at any residue from position 233 (138 residues in length) to 258 (113 residues in length), as position 370 is the end of the C-terminus of the zvegf4 molecule. As such, Gilbert identifies 26 specific polypeptide fragments and dimers thereof, including a polypeptide dimer comprising residues 247-370 of the present SEQ ID NO:2. Although Gilbert does not subject the polypeptide dimer to reducing conditions to reveal the peptide fragments of the dimer as bands I, II and III on SDS-PAGE as that in the instant application, it would have been the inherent property for Gilbert's peptide dimer because it

comprises the polypeptide chains having the same sequence structure as that of the instant invention.

At page 7 of the response, the applicant argues that there are multiple factors involved in generating a bioactive PDGF-D peptide dimmer composition as encompassed by the present claims, and the ordinary skilled artisan would have no reasonable expectation of success, that the Examiner has not supported such a position whether any particular PDGF-D peptide dimmer would have the same bioactivity, and that it is not scientifically possible to predict which of Gilbert's fragments would be bioactive. This argument is not persuasive because it is irrelevant as Gilbert expressly teaches the peptide dimer comprising the same polypeptide chains as that of the present invention. Therefore, the reference anticipates the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 71 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert et al., US 6,495,668 B1, as applied to claims 1, 2, and 66-69 above, and further in view of Invitrogen's "Expressions" (June 1999, Vol. 6 (4), page 6.3-3).

The teachings of Gilbert are reviewed in the previous Office Actions. Gilbert also teaches that polypeptides of the invention can be prepared with changes that do not significantly

affect the folding or activity of the protein or polypeptide, and include an amino- or carboxyl terminal affinity tag, and two or more affinity tags may be used in combination (column 14, lines 29-41), and such include a 6-residue polyhistidine tag (column 15, lines 6-18).

Gilbert does not teach explicitly that the two tags are V5 and His6 tag.

The Invitrogen reference teaches a high level expression vector comprising a C-terminal V5 epitope and a C-terminal His6, wherein V5 epitope is for rapid, low-back ground detection of fusion protein with an anti-V5 antibody, and His6 is for simple purification of fusion proteins.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to generate a fusion protein comprising said polypeptide (taught by Gilbert) fused with two tags such as V5 and His6 tag using the expression vector taught by the Invitrogen reference. The person of ordinary skill in the art would have been motivated to make such a fusion protein because of the advantage taught in the Invitrogen reference that V5 epitope is for rapid, low-back ground detection, and His6 is for simple purification, and reasonably would have expected success because it such tags are well established for their application, and are widely and successfully used in the field.

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Brenda Brumback

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Dong Jiang, Ph.D.
Patent Examiner
AU1646
5/26/05